APPENDIX A
EXPOSURE GUIDELINES FOR INHALATION EXPOSURE TO CHLORINE

1.0 OVERVIEW

1.1 Effects of Exposure

Numerous public health agencies have reviewed available toxicity information on the hazards associated with inhalation exposure to chlorine (Cl_2) and have compiled summaries of the key findings from studies in humans and animals (NIOSH 1976, OSHA 1978, EPA 2000, NRC 2004, AIHA 2004, ATSDR 2010, EPA 2013, CalEPA 2014). The following bullets summarize the main conclusions reported in these documents.

- Chlorine is highly reactive and readily reacts with all organic and many inorganic substances (NRC 2004, ATSDR 2010).
- Chlorine is readily soluble in water and exposure to chlorine in air tends to have the greatest effects on moist tissue surfaces including eyes and the epithelial layer of the respiratory tract (NIOSH 1976, EPA 2000, NRC 2004, ATSDR 2010).
- The odor threshold for chlorine varies between individuals, but is generally between 0.02 and 0.2 ppm (OSHA 1978).
- Some people report a mild "tickling" of nose or throat at concentrations of 0.01 to 0.1 ppm (EPA 2000). Nasal irritation, lacrimation, sore throat and coughing often begin to occur at a concentration of about 0.5-5 ppm, depending on the duration of exposure (OSHA 1978, EPA 2000). These effects are generally transient and usually resolve within several hours after exposure ceases (EPA 2000).
- At higher exposures (generally in the 5-30 ppm range, depending on exposure duration), eye and throat irritation become more severe (OSHA 1978), and necrosis of respiratory epithelial cells may occur (CalEPA 2014). In some cases, pulmonary edema may occur, resulting in symptoms of chest pain and difficult breathing, often with a feeling of choking or suffocation (EPA 2000). Such symptoms may endure several days after cessation of exposure.
- Inhalation exposure to chlorine can be lethal, but the concentration levels causing lethality are not well documented in humans. In animals, the probability of lethality depends both on concentration and duration of exposure, with LC50 values generally in the 300-1,000 ppm range, depending on exposure duration (ATSDR 2010).

1.2 Exposure-Time Relationships

Available toxicity data in humans and animals clearly indicate that the effects of exposure to chlorine depend both on exposure concentration and duration of exposure. Given information of the effect of exposure to concentration "C" for some time interval "t", extrapolation to some other exposure duration is often achieved by assuming that that Haber's Rule applies, which states that the effects of two exposure events will be similar when the product of concentration and time is a constant:

$$C \times t = k$$

For example, if Haber's Rule applies, exposure to 10 ppm for 10 minutes would be expected to produce the same effect as exposure to 1 ppm for 100 minutes or 0.1 ppm for 1,000 minutes. However, studies by ten Berge et al. (1986) indicate that Haber's Rule may not apply to some acute irritants, and that the relationship between exposure level and exposure duration is often better characterized as:

$$C^n \times t = k$$

In such a case, exposure to 10 ppm for 10 minutes is no longer expected to be equally toxic as exposure to 0.1 ppm for 1,000 minutes, which means that it is important to consider the value of n when using toxicity data at one exposure duration to extrapolate to some other exposure duration. Both NAS (2004) and EPA (2013) have reviewed the available literature on the concentration-time relationship for chlorine to determine the value of the exponent "n". Although there is variability between studies, both NAS (2004) and EPA (2013) concluded that a value of $n = 2$ is most appropriate. This value is also used by CalEPA (2014).

2.0 HUMAN EXPOSURE GUIDELINES FOR CHLORINE

2.1 Summary of Human Exposure Guidelines

Numerous health agencies have derived guidelines for human exposure to chlorine.

Table A 2-1 summarizes values for short-term (10 minute to 8 hour) exposures, along with information on the basis of the guideline (when available). These guidelines are best thought of as being protective for single exposure events, with a frequency of repeated exposure that is sufficiently low that any effects from one exposure are fully reversed before a repeat exposure occurs.

Table A 2-2 summarizes guidelines that are intended to be applicable to repeated workplace exposures or longer term continuous exposures.

In several cases (NAS AEGLs, AIHA ERPGs, CalEPA acute RELs, EPA PALs), guidelines were developed for two or three differing severity levels of adverse effect. Although definitions of the tiers vary somewhat between agencies, the severity tiers may be thought of as follows:

- Tier 1 guidelines identify the threshold for relative mild and reversible effects
- Tier 2 guidelines identify the threshold for more substantial but still reversible effects
- Tier 3 guidelines represent thresholds for serious and potentially disabling or life-threatening exposures.

Figure A 2-1 provides a graphical summary of the short-term and long-term guideline values, plotted as a function of exposure duration and stratified by the severity level associated with the guideline. As seen, values for similar durations and severity levels may differ somewhat between agencies due to differences in the data considered to be the best starting point, the methods used to extrapolate over time, and the application of uncertainty factors. Nevertheless, there is relatively good agreement between most guidelines.

2.2 Choice of Guidelines for Evaluation of Human Health Risks at the U.S. Magnesium Site

In selecting the most appropriate human exposure guidelines for use at the U.S. Magnesium site, two factors were considered to be important:

- Guidelines based on data from intermittent exposures that require extrapolation across time should be derived using the relationship recommended by ten Berge et al (1986) with an exponent of 2.
- Guidelines should be available for a range of exposures durations and for several severity levels to allow a proper characterization of risks and to support well-informed risk management decision-making.

Based on these criteria, the following guidelines were identified as being most appropriate:

- Short-term Exposures: NAS AEGL values
- Longer-term Exposures: EPA PALs
- Chronic Exposure: ATSDR Chronic MRL. Although this value is derived using Haber's Rule (n = 1), the application of uncertainty factors in the derivation of the MRL likely accounts for any underestimation that might result.

These values are summarized in Table A 2-3.

Table A 2-1. Short-Term Human Exposure Guidelines

Agency	Guideline	Key Studies	Exposed Organisms	Expiosure Duration	Critical Effect	NOEC ppm	LOEC ppm	POD ppm	POD Note	Adjustments $C^n * t = k$	Adjustments Interspecies	Adjustments UF	Value (ppm) 10-15 min	Value (ppm) 30 min	Value (ppm) 1 hr	Value (ppm) 4 hr	Value (ppm) 8 hr
NIOSH	IDLH	Freitag 1941	Humans	1-1.5 hrs	Lethality		34-51	10						10			
	Short term REL	Rupp and Henschler 1967 Beck 1959, Matt 1889 Patil et al 1970	Humans	<= 1 hr	Occular and respiratory irritation		0.2 - 1.3	0.5					1.0				
OSHA	Short term PEL	Anglen 1981 Rotman et al. 1983	Humans	8 hrs	Sensory irritation, decreased pulmonary function	0.5	1						1.0				
ACGIH	STEL												1.0				
NAS	AEGL 1	D'Alessandro et al 1996 Rotman et al 1983 Shusterman et al. 1998	Human (including sensitive individuals)	15 min - 8 hr	Transient nonsymptomatic changes in pulmonary air flow	0.4 - 0.5		0.5		n=2			0.5	0.5	0.5	0.5	0.5
	AEGL 2	D'Alessandro et al 1996 Rotman et al 1983	Human (including sensitive individuals)	4 hr	Shortness of breath, wheezing, increase resistance to airflow	1.0		1.0		n=2		1	2.8	2.8	2.0	1.0	0.7
	AEGL 3	MacEwen and Vernort 1972 Zwart and Woutersen 1988	Rat	1 hr	Lethality	213, 322		200		n=2		9	50	28	20	10	7.1
			Mouse	1 hr	Lethality		150										
CalEPA	Acute REL (mild)	Anglen 1981	Human	30 min	Itching and burning throat	1.0				n=2		10			0.07		
	Acute REL (severe)	D'Alessandro et al 1996	Human	1 hour	Decreased FEV	0.4	1.0	0.4							0.4		
	Acute REL (life-threatening)	Zwart and Woutersen 1988	Rat	1 hour	Lethality			311				30			10		
AIHA	ERPG 1	Rotman et al. 1983 D'Alessandro et al 1996	Human	4 hours	Sensory irritation Changes in pulmonary function	0.4 - 1									1		
	ERPG 2	Rotman et al. 1983	Human	1 hour	Transient changes in pulmonary function										3		
	ERPG 3	Demnati et al 1995 NTIS 1972	Rats	1 hour	Lethality	200-293									20		

Table A 2-2. Repeat Exposure and Longer-Term Human Exposure Guidelines

Agency	Guideline	Applicable Duration	Key Studies	Exposed Organisms	Expiosure Duration	Critical Effect	NOEC ppm	LOEC ppm	POD ppm	Adjustments Haber	Adjustments HEC	Adjustments UF	Value (ppm) (ppm)
NIOSH	REL	repeated 8-hour exposures	Rupp and Henschler 1967 Beck 1959, Matt 1889 Patil et al 1970	Humans	8 hrs	Sensory irritation, decreased pulmonary function							0.5
OSHA	PEL	repeated 8-hour exposures	Anglen 1981 Rotman et al. 1983	Humans	8 hrs	Isensory irritation, decreased pulmonary function							0.5
ACGIH	TWA	repeated 8-hour exposures											0.5
ATSDR	Acute MRL	continuous for up to 14 days	Multiple (Anglen 1981, D'Alessandro et al 1996, Rotman et al. 1983, Schins et al, 2000)	Human	8 hr	Irritation of eyes, nose and throat; transient increased airway resistance.	0.5	1	0.5	n=1		3	0.06
	Intermediate MRL	continuous for 2 wks to 1 yr	Kutzman 1983	Rats	6 hr/day, 5 d/wk, 9 wks	Loss of cilia and epithelium in trachea	--	0.5	0.5	n=1		90	0.001
	Chronic MRL	Continuous for a lifetime	Klonne et al. 1987	Monkey	6 hr/day, 5 day/wk, 1 yr	focal epithelial hyperplasia in nose and trachea	--	0.1	0.02	n=1		60	0.00005
EPA NHSRC	PAL-1	Continuous, 1 day	Rotman et al. 1983	Human	8 hrs	Decreased pulmonary function Eye, nose, and throat irritation	0.5	1	0.29	n=2		3	0.096
		Continuous, 30 day	Jarabek 2013	Rats	6 hrs/day 5 days/wk 2 weeks	Nasal lesions	0.1	1	0.18	n=2		9	0.018
		Continuous, 90 day	Klonne et al. 1987	Monkey	6 hrs/day 5 days/wk 1 year	Nasal lesions	0.1	2.3	0.036	n=2		9	0.0036
		Continuous, 2 year	Klonne et al. 1987	Monkey	6 hrs/day 5 days/wk 1 year	Nasal lesions	0.1	2.3	0.036	n=2		9	0.0036
	PAL-2	Continuous, 1 day	Anglen 1981 Rotman et al. 1983	Human	8 hrs	Decreased pulmonary function Eye, nose, and throat irritation	0.5	1	0.58	n=2		3	0.19
		Continuous, 30 day	One third of 30-day PAL-3	Rats					0.32	n=2		3	0.11
		Continuous, 90 day	CIIT 1994 Wolf et al. 1995	Mice	6 hrs/day 5 days/wk 2 years	Decreased body weight Mild to moderate nasal lesions	0.4	1	0.36	n=2		9	0.036
		Continuous, 2 year	CIIT 1994 Wolf et al. 1995	Mice	6 hrs/day 5 days/wk 2 years	Decreased body weight Mild to moderate nasal lesions	0.4	1	0.36	n=2		9	0.036
	PAL-3	Continuous, 1 day	Weedon et al. 1940	Rats Mice	16 hours	Lethality	63	250	51.4	n=2		9	5.1
		Continuous, 30 day	Barrow et al. 1979	Rats	6 hrs/day 5 days/wk 6 weeks	Severe respiratory irritation Threshold for lethality	3	9	3.2	n=2		9	0.32
		Continuous, 90 day	Barrow et al. 1979	Rats	6 hrs/day 5 days/wk 6 weeks	Severe respiratory irritation Threshold for lethality	3	9	3.2	n=2		9	0.32
CalEPA	Chronic REL	Continuous for a lifetime	Wolf et al. 1995	Rats	6 hrs/day 3 days/wk 2 years	Respiratory epithelial lesions		0.4	0.14	n = 1	0.16	30	0.00008

Figure A 2-1 Human Exposure Guidelines

MILD (Blue Diamnods)

Time	Value (min)	ppm	ug/m3	Source
8 hrs	480	0.5	1450	NIOSH REL
15 min	15	1.0	2900	NIOSH STEL
8 hrs	480	0.5	1450	OSHA PEL
15 min	15	1.0	2900	ACGIH STEL
8 hrs	480	0.5	1450	ACGIH TLV
10 min	10	0.5	1450	AEGL1
30 min	30	0.5	1450	AEGL1
60 min	60	0.5	1450	AEGL1
4 hrs	240	0.5	1450	AEGL1
8 hrs	480	0.5	1450	AEGL1
1 hrs	60	0.07	203	CalEPA REL
1 hrs	60	1.0	2900	AIHA ERPG 1
14 days	20160	0.06	174	ATSDR Acute MRL
1 years	525600	0.001	2.9	ATSDR Intermediate MRL
70 years	36792000	0.00005	0.1	ATSDR Chronic MRL
70 years	36792000	0.0008	2.3	CalEPA Chronic REL
24 hrs	1440	0.096	278	PAL-1
30 days	43200	0.018	52	PAL-1
90 days	129600	0.0036	10	PAL-1
2 years	1051200	0.0036	10	PAL-1

MODERATE (Yellow squares)

Time	Value (min)	ppm	ug/m3	Source
10 min	10	2.8	8120	AEGL 2
30 min	30	2.8	8120	AEGL 2
60 min	60	2	5800	AEGL 2
4 hrs	240	1	2900	AEGL 2
8 hrs	480	0.7	2030	AEGL 2
60 min	60	0.4	1160	CalEPA REL
60 min	60	3	8700	AIHA ERPG 2
24 hrs	1440	0.19	551	PAL-2
30 days	43200	0.11	319	PAL-2
90 days	129600	0.036	104	PAL-2
2 years	1051200	0.036	104	PAL-2

SEVERE (red triangles)

Time	Value (min)	ppm	ug/m3	Source
30 min	30	10	29000	IDLH
10 min	10	50	145000	AEGL 3
30 min	30	28	81200	AEGL 3
60 min	60	20	58000	AEGL 3
4 hrs	240	10	29000	AEGL 3
8 hrs	480	7.1	20590	AEGL 3
60 min	60	10	29000	CalEPA REL
60 min	60	20	58000	AIHA ERPG 3
24 hrs	1440	5.1	14790	PAL-3
30 days	43200	0.32	928	PAL-3
90 days	129600	0.32	928	PAL-3

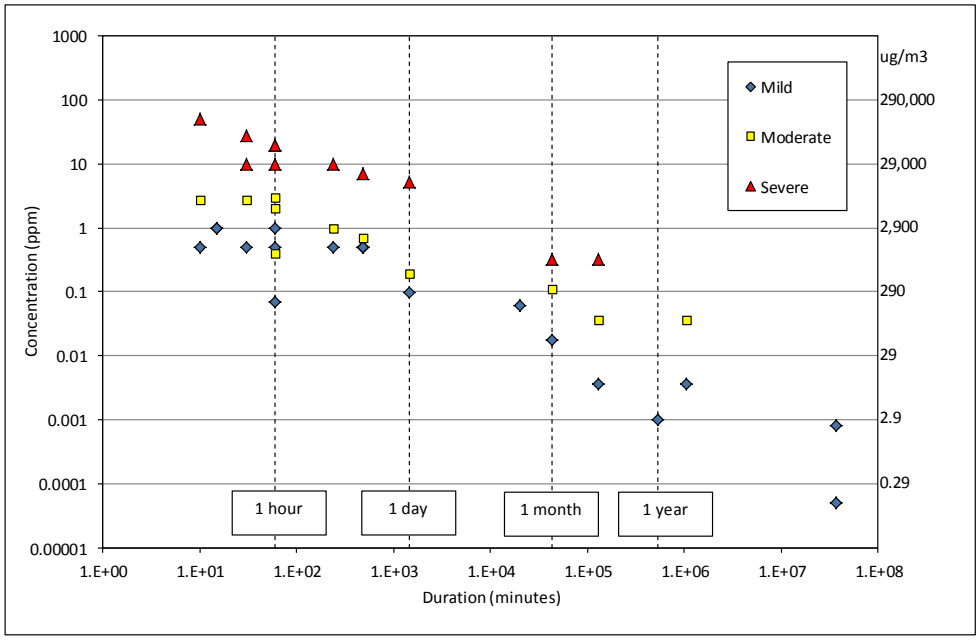

Table A 2-3 Selected Human Exposure Guidelines for Chlorine

Panel A: AEGL Values for Short-Term Exposure (ppm)

Exposure Duration	Severity		
	AEGL-1 (Mild)	AEGL-2 (Moderate)	AEGL-3 (Severe)
10 min	0.5	2.8	50
30 min	0.5	2.8	28
1 hr	0.5	2.0	20
4 hr	0.5	1.0	10
8 hr	0.5	0.7	7.1

Panel B: PAL Values for Longer-Term Exposure (ppm)

Exposure Duration	Severity		
	PAL-1 (Mild)	PAL-2 (Moderate)	PAL-3 (Severe)
24 hr	0.096	0.19	5.1
30 days	0.018	0.11	0.32
90 days	0.0036	0.036	0.32
2 years	0.0036	0.036	--

Panel C: Chronic Exposure

ATSDR Chronic MRL: 0.00005 ppm

3.0 ECOLOGICAL EXPOSURE GUIDELINES FOR CHLORINE

No existing guidelines were located for exposure of ecological receptors (mammals, birds) to chlorine. The following section summarizes studies that were used to derive Toxicity Reference Values (TRVs) for birds and mammals at this site.

3.1 Mammals

Lethality

Inhalation exposure to high level of chlorine can be lethal in mammals. Figure A 3-1 summarizes LC50 data from a number of studies. As shown, the values tend to decrease as exposure duration increases, with most values in the 300-1000 ppm range.

According to Rusch (2000), an LC(low) (the threshold effect level for lethality) can be estimated from an LC50 by dividing by a factor of 3. Based on this, TRVs for protection against lethality may be estimated to be approximately 300 ppm for an exposure duration of 10-30 minutes and approximately 100 ppm for an exposure duration of 6-8 hours.

No studies were located that provide sufficient data to identify an LC50 or an LC(low) following repeated exposures. In the absence of data, a value is estimated by dividing the LC(low) for 6-8 hours exposure by an uncertainty factor of 3.

These TRVs for lethality in mammals are summarized below:

Duration	Frequency	TRV (ppm)
10 minutes	Infrequent	300 ppm
6 hrs	Infrequent	100 ppm
6 hrs	Repeated	30 ppm

Systemic Effects

The primary systemic effects of chlorine exposure in mammals is irritation of eyes and nose at low level exposures with damage to the cells of the respiratory tract and altered respiratory function at higher exposures. While low level of exposures that cause only mild irritation are not likely to cause ecologically significant effects, more serious effects on the nose or respiratory system might interfere with the ability to locate and capture prey and/or avoid predation. Consequently, TRVs for systemic effects are based on serious effects on the nose of respiratory tract.

Single Exposures

Table A 3-1 summarizes a number of short-term (5 minute to 6 hour) studies on the effects of inhalation of chlorine by mammals. The data are illustrated graphically below the table. As shown, for short-term exposures in the range of 10-30 minutes, serious effect levels occurred at exposure concentrations of about 100 ppm. To move from a serious effect level to a threshold for serious effects, the value of 100 ppm is divided by a factor of 3, resulting in a TRV of 30 ppm.

No studies were located to identify a serious effect level for a short-term exposure of 6-8 hours duration, so a TRV value for this duration was estimated based on the exposure-duration model recommended by ten Berge et al. (1986), and assuming an exponent of 2:

$$\text{TRV(6 hrs)} = [\ \text{TRV(30 minutes)}^2 \quad (0.5 / 6)\ ]^{0.5}$$
$$= [30^2 / 12\ ]^{0.5} = 8.7 \text{ ppm (rounded to 9 ppm)}$$

Repeated Exposures

Table A 3-2 summarizes studies in which mammals underwent repeated exposure to chlorine. As indicated, several studies found that repeated exposure 6 hrs/day to 9-12 ppm resulted in relatively significant effects that might be associated with decreased chances of survival in the wild.

Based on this, TRVs for protection of mammals against serious systemic effects from repeated exposures (6 hrs in duration) to chlorine may be estimated to be approximately 9 ppm. To move from a serious effect level to a threshold for serious effects, the value of 9 ppm is divided by a factor of 3, resulting in a TRV of 3 ppm. This value is consistent with several other studies that reported that repeated exposures ranging from 9 weeks to 2 years to concentrations in the range of 0.5 to 2.5 ppm caused either no effects or only mild effects that would not be likely to result in decreased growth, survival or reproduction.

Summary of TRVs for Mammals

Table A 3-3 (upper section) summarizes the TRVs derived for mammals that have been selected for use at the U.S. Magnesium site.

3.2 Birds

No quantitative data were located on the effects of chlorine on birds. In the absence of data, values for birds were derived from value for mammals by dividing by an uncertainty factor of 3. These values are summarized in Table A 3-3 (lower section). Although the resultant values are

considered to be uncertain, it is nevertheless expected that if exposure levels do not exceed the TRVs, population-level effects are unlikely to be ecologically significant.

Figure A 3-1. LC50 Values in Mammals

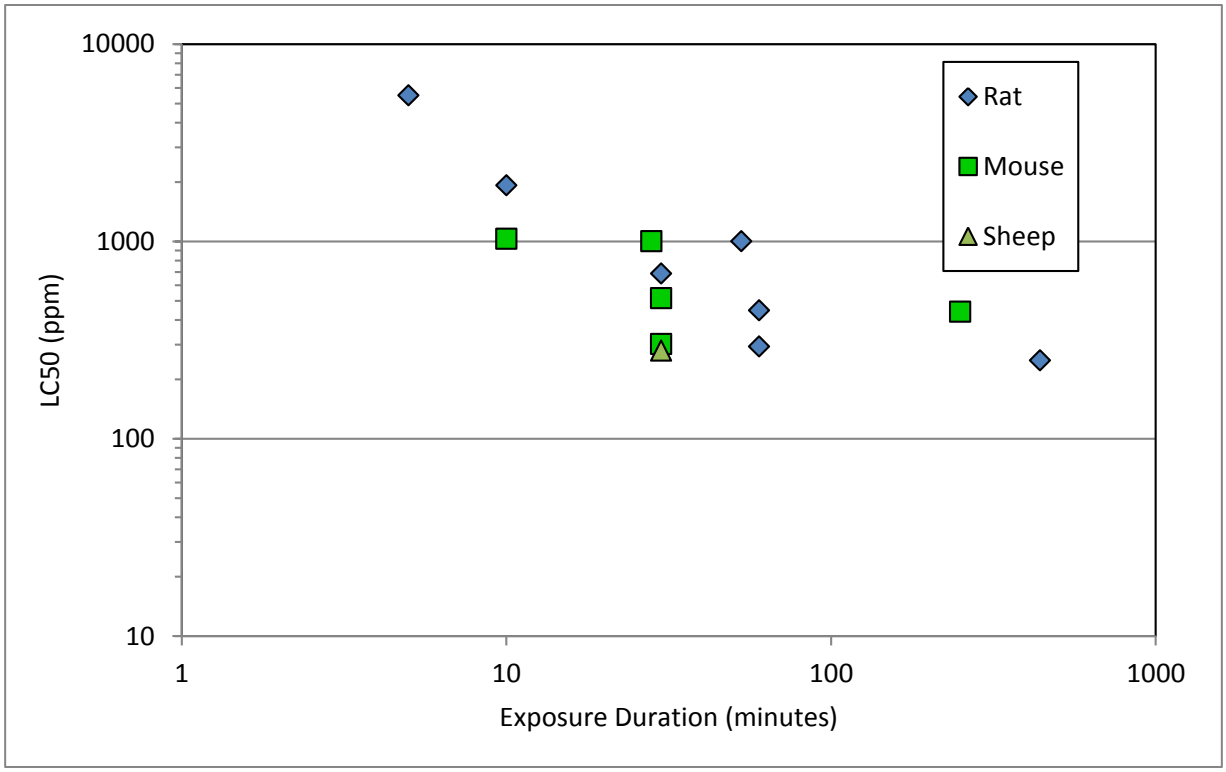

Table A 3-1. Systemic Effects of Short-term Exposures to Mammals

Reference	Species	Endpoint	ET (min)	NOEC	LOEC(mild)	LOEC(serious)
Barrow and Steinhagen 1982	Rat	Decreased resp rate	10		25	
Demnati et al 1995	Rat	Slight edema	10	100	200	
Leustik et al 2008	Rat	Histolog/biochem evidnce of lung injury	30		184	
McNulty et al 1983	Rat	Decreased -SH in nasal epithelium	360	2.5	5	
Yildirim et al 2004	Rat	Pulmonara edema & hemorrhage	15			1330
Barrow et al 1977	Mouse	Decreased rep. rate	10		1.8	
Gagnaire et al 1994	Mouse	Decreased rep. rate	60		3.5	
Martin et al 2003	Mouse	Flattening of pulmonary epithelium	5		100	
Morris et al 2005	Mouse	Decreased rep. rate	15		2.3	
Tian et al 2008	Mouse	Histolog/biochem evidnce of lung injury	60		221	
Barrow and Smith 1975	Rabbit	Pulmonara edema, emphysema	30			100
Batchinsky et al 2006	Sheep	Immediate and sustained lung injurt	30			120
Hoyle 2010	Mouse	Decreased rep. rate	60		100	
Wang 2005	Pig	Reduced air flow, reduced blood oxygen	15			400

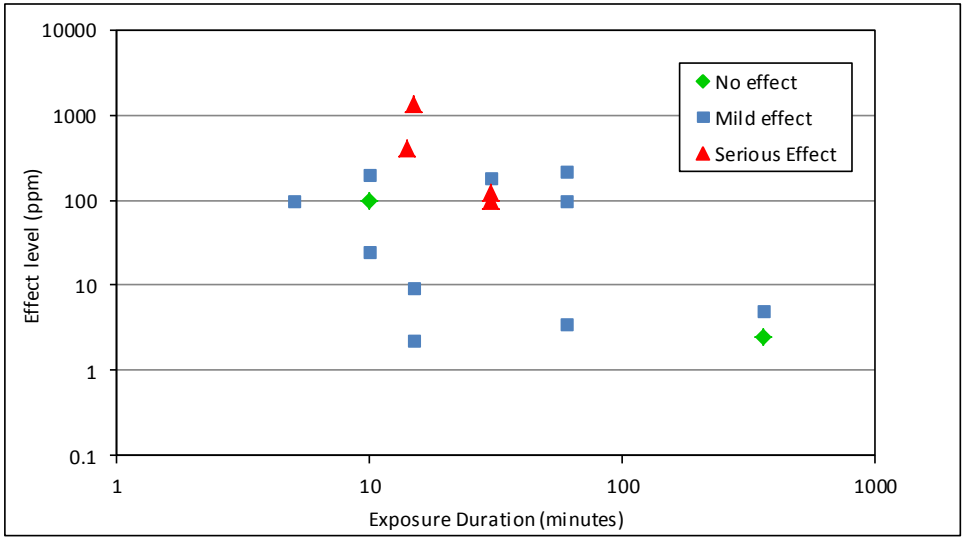

Table A 3-2. Systemic Effects of Repeated Exposures of Mammals

Reference	Species	Endpoint	ET (hrs/day)	EF (days/week)	ED (weeks)	NOEC (ppm)	Mild LOEC (ppm)	Serious LOEC (ppm)
Jiang et al 1983	Rat	Erosion of olfactory epithelium, wt loss	6	5	1	--	--	9.1
Buckley et al 1984	Mouse	Erosion and ulceration of resp epithelium	6	5	1	--	--	9.3
Jiang et al 1983	Mouse	Erosion of olfactory epithelium, wt loss	6	5	1	--	--	9.1
Dodd et al 1980	Rat	Wheezing, nasal & ocular irritation, wt loss	6	5	2	--	--	12
Kutzman 1983	Rat	Loss of epithelia cillia	6	5	9	--	0.5	--
Barrow et al 1979	Rat	Nasal inflamation	6	5	9	--	1.0	--
Klonne et al. 1987	Monkey	Focal nasal and tracheal hyperplasia	6	5	52	0.5	2.3	--
Wolf 1995	Mouse	Nasal lesions, decreased BW	6	5	104	0.4	1.0	--
Wolf 1995	Rat	Nasal lesions, decreased BW	6	5	104	0.4	1.0	--

Table A 3-3.
Selected TRVs (ppm) for Exposure of Ecological Receptors to Cl_2

Receptor Group	Exposure Duration	Exposure Frequency	Endpoint	
			Nasal/Resp. Tract Injury	Lethality
Mammals	10-30 min	Infrequent	30	300
	6-8 hr	Infrequent	9	100
	6-8 hr	Repeated	3	30
Birds	10-30 min	Infrequent	10	100
	6-8 hr	Infrequent	3	30
	6-8 hr	Repeated	1	10

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APPENDIX B
HEATH EFFECTS DATA AND EXPOSURE GUIDELINES FOR INHALATION EXPOSURE TO HYDROCHLORIC ACID

1.0 OVERVIEW

Several public health agencies have reviewed available toxicity information on the hazards associated with inhalation exposure to hydrochloric acid (HCl) and have compiled summaries of the key findings from studies in humans and animals (EPA 2000, CalEPA 2000, CalEPA 2008, AIHA 2008, EPA 2009, NRC 2004). The following bullets summarize the main conclusions reported in these documents.

- Hydrochloric acid is corrosive to the eyes, skin, and mucous membranes. Acute inhalation exposure may cause coughing, hoarseness, inflammation and ulceration of the respiratory tract, chest pain, and pulmonary edema in humans (EPA 2000, CalEPA 2008)
- Chronic occupational exposure to hydrochloric acid has been reported to cause gastritis, chronic bronchitis, dermatitis, and photosensitization. Prolonged exposure to low concentrations may also cause dental discoloration and erosion (EPA 2000, CalEPA 2000)
- HCl is a sensory and respiratory irritant and causes changes in the upper respiratory tract, with the severity depending on concentrations and exposure duration. As concentrations and exposure times increase, effects progress to the lower respiratory tract and may involve pulmonary edema and histopathologic changes (NRC 2004, EPA 2009).
- Chronic inhalation exposure of rats caused hyperplasia of the nasal mucosa, larynx, and trachea and lesions in the nasal cavity (EPA 2000, EPA 2009)

1.2 Exposure-Time Relationships

Available toxicity data in humans and animals clearly indicate that the effects of inhalation exposure to HCl depend both on exposure concentration and duration of exposure. Given information of the effect of exposure to concentration "C" for some time interval "t", extrapolation to some other exposure duration is often achieved by assuming that that Haber's Rule applies, which states that the effects of two exposure events will be similar when the product of concentration and time is a constant:

$$C \times t = k$$

For example, if Haber's Rule applies, exposure to 10 ppm for 10 minutes would be expected to produce the same effect as exposure to 1 ppm for 100 minutes or 0.1 ppm for 1,000 minutes. Studies by ten Berge et al. (1986) indicate that Haber's Rule may not apply to some acute

irritants, and that the relationship between exposure level and exposure duration is often better characterized as:

$$C^n \times t = k$$

Both NAS (2004) and EPA (2013) have reviewed the available literature on the concentration-time relationship for HCl to determine the value of the exponent "n". Although there is variability between studies, both NAS (2004) and EPA (2013) concluded that a value of n = 1 is most appropriate (i.e., Haber's Rule is applicable).

2.0 HUMAN EXPOSURE GUIDELINES FOR HCl

2.1 Summary of Human Exposure Guidelines

Numerous health agencies have derived guidelines for human exposure to chlorine.

Table B 2-1 summarizes values for short-term (10 minute to 8 hour) exposures, along with information on the basis of the guideline (when available). These guidelines are best thought of as being protective for single exposure events, with a frequency of repeated exposure that is sufficiently low that any effects from one exposure are fully reversed before a repeat exposure occurs.

Table B 2-2 summarizes guidelines that are intended to be applicable to repeated workplace exposures or longer term continuous exposures.

In several cases (NAS AEGLs, AIHA ERPGs, CalEPA acute RELs, EPA PALs), guidelines were developed for two or three differing severity levels of adverse effect. Although definitions of the tiers vary somewhat between agencies, the severity tiers may be thought of as follows:

- Tier 1 guidelines identify the threshold for relative mild and reversible effects
- Tier 2 guidelines identify the threshold for more substantial but still reversible effects
- Tier 3 guidelines represent thresholds for serious and potentially disabling or life-threatening exposures.

Figure B 2-1 provides a graphical summary of the short-term and long-term guideline values, plotted as a function of exposure duration and stratified by the severity level associated with the guideline. As seen, values for similar durations and severity levels may differ somewhat between agencies due to differences in the data considered to be the best starting point, the methods used to extrapolate over time, and the application of uncertainty factors. Nevertheless, there is relatively good agreement between most guidelines.

2.2 Choice of Guidelines for Evaluation of Human Health Risks at the U.S. Magnesium Site

In selecting the most appropriate human exposure guidelines for use at the U.S. Magnesium Site, two factors were considered to be important:

- Guidelines based on data from intermittent exposures that require extrapolation across time must be derived using the relationship recommended by ten Berge et al (1986) with an exponent of 1.
- Guidelines must be available for a range of exposures durations and for several severity levels to allow a proper characterization of risks and to support well-informed risk management decision-making.

Based on these criteria, the following guidelines were identified as being most appropriate:

- Short-term Exposures: NAS AEGL values
- Longer-term Exposures EPA PALs
- Chronic Exposure: EPA RfC

These values are summarized in Table B 2-3.

Table B 2-1. Short-Term Human Exposure Guidelines

Agency	Guideline	Key Studies	Exposed Organisms	Expiosure Duration	Critical Effect	NOEC ppm	LOEC ppm	POD ppm	POD Note	Adjustments Interspecies	Adjustments UF	Value (ppm) 10-15 min	Value (ppm) 30 min	Value (ppm) 1 hr	Value (ppm) 4 hr	Value (ppm) 8 hr
NIOSH	IDLH	Flury and Zernik 1931 Henderson and Haggard 1943 Tab Biol Per 1933	Human		Inability to work at 50 ppm		50						50			
NAS	AEGL 1	Stevens et al. 1992	Humans	45 min	Upper resp symptoms	1.8	--				1	1.8	1.8	1.8	1.8	1.8
	AEGL 2	Stavert et al. 1991	Rat	30 min	Severe nasal and pulmonary histopathology	--	1300				30	100	43	22	11	11
	AEGL 3	Wohlslager et al. 1976 Vernot et al. 1977	Rat	1 hr	Lethality		LC50 = 3124	1000	a		10	620	210	100	26	26
CalEPA	Acute REL (mild)	Stevens et al. 1992	Humans	45 min	Upper resp symptoms	1.8	--	1.4			1			1.4		
	Acute REL (severe)	NRC 1987	Mice	10 min			RD50 = 309				~15			20		
	Acute REL (life-threatening)	Hartzell et al. 1985	Rat	1 hr	Lethality	1800.0	2280	1270	b		30			42		
AIHA	ERPG 1	Stevens et al. 1992	Humans	45 min	Upper resp symptoms	1.8	--							3		
	ERPG 2	Multiple	Humans Animals		Serious eye and respiratory btract injury	20								20		
	ERPG 3	Multiple	Animals	15 min - 6 hr4	Lethality	150								150		

a LClow = LC50 / 3
b BMCL

Table B 2-2. Repeat Exposure and Longer-Term Human Exposure Guidelines

Agency	Guideline	Applicable Duration	Key Studies	Exposed Organisms	Exposure Duration	Critical Effect	NOEC ppm	LOEC ppm	POD ppm	Adjustments HEC	Adjustments UF	Value (ppm) (ppm)
NIOSH	REL	repeated 8-hour exposures										5.0
OSHA	PEL	repeated 8-hour exposures										5.0
ACGIH	TWA	repeated 8-hour exposures										5.0
EPA NHSRC	PAL-1	Continuous, 1 day	Srevens et al. 1992	Human	45 min	Irritation	1.8					1.8
		Continuous, 30 day	Toxigenics Inc 1984	Rats	6 hr/day 5 day/wk 90 days	Decreased body weight Minimal to mild histopathological of nasal cavity		50	8.9		10	0.9
		Continuous, 90 day	Toxigenics Inc 1984	Rats	6 hr/day 5 day/wk 90 days	Decreased body weight Minimal to mild histopathological of nasal cavity		50	8.9		10	0.9
		Continuous, 2 year	Sellakumar et al 1994 Albert et al. 1982	Rat	6 hr/day 5 day/wk Lifetime	No effect on body weight or survival	10		1.8		10	0.18
	PAL-2	Continuous, 1 day	Henderson and Haggard 1943	Human	24 hr	Maximum tolerable exposure	10				1	10
		Continuous, 30 day	Henderson and Haggard 1943	Human	24 hr	Maximum tolerable exposure	10				3	3.3
		Continuous, 90 day	Henderson and Haggard 1943	Human	24 hr	Maximum tolerable exposure	10				3	3.3
		Continuous, 2 year										--
	PAL-3	Continuous, 1 day	Wohlslagel et al. 1976	Rat	1 hour	Threshold for lethality		1774	73.9		3	25
		Continuous, 30 day										--
		Continuous, 90 day										--
EPA	RfC	Continuous for a lifetime	Sellakumar et al 1994 Albert et al. 1982	Rat	6 hr/eday 5 day/wk Lifetime	Hyperplasia of eipitelial cells in nose and upper respiratory tract		10		0.442	300	0.013
CalEPA	Chronic REL	Continuous for a lifetime	Sellakumar et al 1985	Rat	6 hr/day 5 day/wk Lifetime	Hyperplasia of eipitelial cells in nose and upper respiratory tract		1.8		0.32	100	0.006

DRAFT -- FOR DISCUSSION PURPOSES

Figure B 2-1 Human Exposure Guidelines

MILD (Blue Diamnods)

Time	(min)	Value ppm	ug/m3	Source
8 hrs	480	5	14500	NIOSH REL
8 hrs	480	5.0	14500	OSHA PEL
8 hrs	480	5	14500	ACGIH TLV
10 min	10	1.8	5220	AEGL1
30 min	30	1.8	5220	AEGL1
60 min	60	1.8	5220	AEGL1
4 hrs	240	1.8	5220	AEGL1
8 hrs	480	1.8	5220	AEGL1
1 hrs	60	1.4	4060	CalEPA REL
1 hrs	60	3.0	8700	AIHA ERPG 1
70 years	36792000	0.013	38.9	EPA RfC
70 years	36792000	0.006	17.4	CalEPA Chronic REL
24 hrs	1440	1.8	5220	PAL-1
30 days	43200	0.9	2610	PAL-1
90 days	129600	0.9	2610	PAL-1
2 years	1051200	0.18	522	PAL-1

MODERATE (Yellow squares)

Time	(min)	Value ppm	ug/m3	Source
10 min	10	100	290000	AEGL 2
30 min	30	43	124700	AEGL 2
60 min	60	22	63800	AEGL 2
4 hrs	240	11	31900	AEGL 2
8 hrs	480	11	31900	AEGL 2
60 min	60	20	58000	CalEPA REL
60 min	60	20	58000	AIHA ERPG 2
24 hrs	1440	10	29000	PAL-2
30 days	43200	3.3	9570	PAL-2
90 days	129600	3.3	9570	PAL-2

SEVERE (red triangles)

Time	(min)	Value ppm	ug/m3	Source
30 min	30	50	145000	IDLH
10 min	10	620	1798000	AEGL 3
30 min	30	210	609000	AEGL 3
60 min	60	100	290000	AEGL 3
4 hrs	240	26	75400	AEGL 3
8 hrs	480	26	75400	AEGL 3
60 min	60	42	121800	CalEPA REL
60 min	60	150	435000	AIHA ERPG 3
24 hrs	1440	25	72500	PAL-3

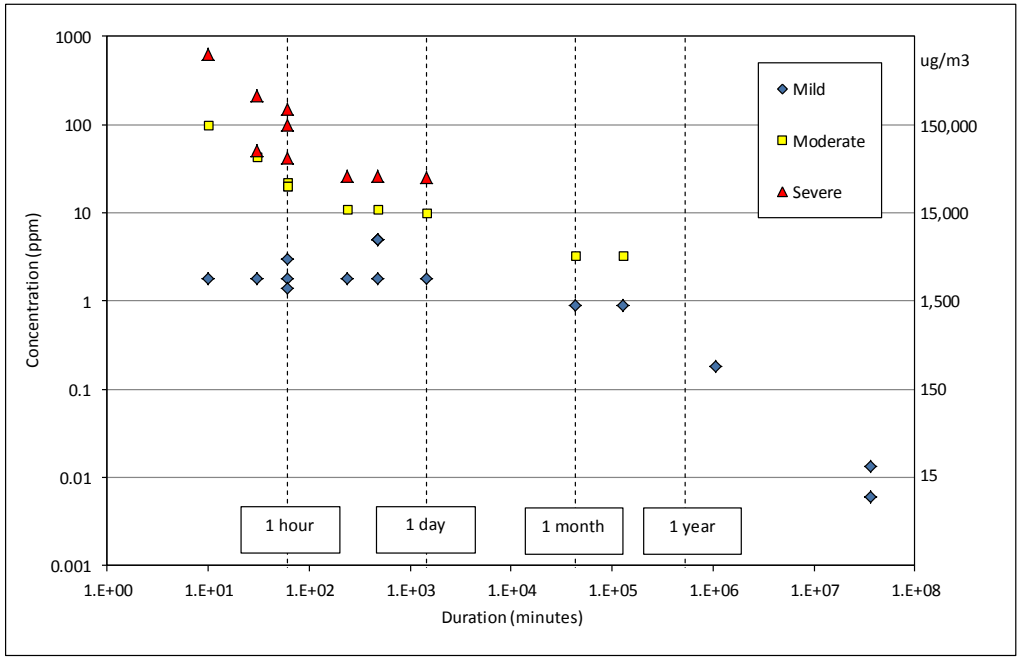

Table B 2-3 Selected Human Exposure Guidelines for HCl

Panel A: AEGL Values for Short-Term Exposure (ppm)

Exposure Duration	Severity		
	AEGL-1 (Mild)	AEGL-2 (Moderate)	AEGL-3 (Severe)
10 min	1.8	100	620
30 min	1.8	43	210
1 hr	1.8	22.0	100
4 hr	1.8	11.0	26
8 hr	1.8	11	26

Panel B: PAL Values for Longer-Term Exposure (ppm)

Exposure Duration	Severity		
	PAL-1 (Mild)	PAL-2 (Moderate)	PAL-3 (Severe)
24 hr	1.8	10	25
30 days	0.9	3.3	--
90 days	0.9	3.3	--
2 years	0.9	--	--

Panel C: Chronic Exposure

EPA RfC: 0.013 ppm (continuous lifetime exposure)

3.0 ECOLOGICAL EXPOSURE GUIDELINES FOR HCl

No existing guidelines were located for inhalation exposure of ecological receptors (mammals, birds) to HCl. The following section summarizes studies that were used to derive Toxicity Reference Values (TRVs) for birds and mammals at this site.

3.1 Mammals

Lethality

Inhalation exposure to HCl can cause severe injury to the lung resulting in lethality. Figure B 3-1 summarizes data from a number of studies in mammals. As shown, there is substantial variation between studies and between species, with mice generally tending to be the most sensitive. Taken together, the data indicate that lethality in mammals is unlikely to occur following exposures of 300 ppm for up to 10 minutes or 100 ppm for exposures of 1-6 hours.

No studies were located that provide sufficient data to identify an LC50 or an LC(low) following repeated exposures. In the absence of data, a value is estimated by dividing the value for 6-8 hours exposure by an uncertainty factor of 3.

These TRVs for lethality in mammals are summarized below:

Duration	Frequency	TRV (ppm)
10 minutes	Infrequent	300 ppm
6 hrs	Infrequent	100 ppm
6 hrs	Repeated	30 ppm

Systemic Effects

<u>Single Exposures</u>

Table B 3-1 summarizes a number of short-term (5-30 minute) studies on the effects of inhalation of HCl by mammals. The data are illustrated graphically below the table. As shown, exposure to concentrations below 100 ppm appear to cause only mild and reversible effects (e.g., mild irritation, altered breathing rate) that are unlikely to cause ecologically significant impacts on growth, reproduction or survival of exposed organisms.

Based on this, the TRV for protection of mammals against serious systemic effects from short-term (10-30 minutes) single exposures to HCl may be estimated to be approximately 100 ppm.

No studies were located to identify a serious effect level for a short-term exposure of 6-8 hours duration, so a TRV value for this duration was estimated based on application of Haber's Rule:

TRV(6 hrs) = TRV(30 minutes) * (0.5 / 6)
= 100 ppm * 0.083 = 8.3 ppm

Repeated Exposures

Table B 3-2 summarizes studies that were located in which mammals underwent repeated exposure to HCl for 6 hours per day for 3 or more days. The data are too limited to draw firm conclusions, but exposure to 309 ppm HCl caused death in exercising guinea pigs after 3 days. In order to be conservative, the TRV for long-term repeated exposure to HCl is derived as follows:

POD = 309 ppm
Haber's Rule Adjustment = 6/24
UF1 = 3 to estimate LD(low) (Rauch et al. 2009)
UF2 = 3 to extrapolate from 3 days to longer term
UF3 = 3 for database limitations

TRV = 309 ppm * (6/24) / 30 = 3 ppm

This value is consistent with the findings reported by Albert et al. (1982) in which only mild effects occurred in rats exposed 6 hr/ day for a lifetime. After application of Haber's rule, this would correspond to 2.5 ppm as mild effect level for continuous exposure.

Summary of TRVs for Mammals

Table B 3-3 (upper section) summarizes the TRVs derived for mammals that have been selected for use at the U.S. Magnesium site.

3.2 Birds

No quantitative data were located on the effects of HCl on birds. In the absence of data, values for birds were derived from value for mammals by dividing by an uncertainty factor of 3. These values are summarized in Table B 3-3 (lower section). Although the resultant values are considered to be uncertain, it is nevertheless expected that if exposure levels do not exceed the TRVs, population-level effects are unlikely to be ecologically significant.

Figure A 3-1. Lethality Values in Animals

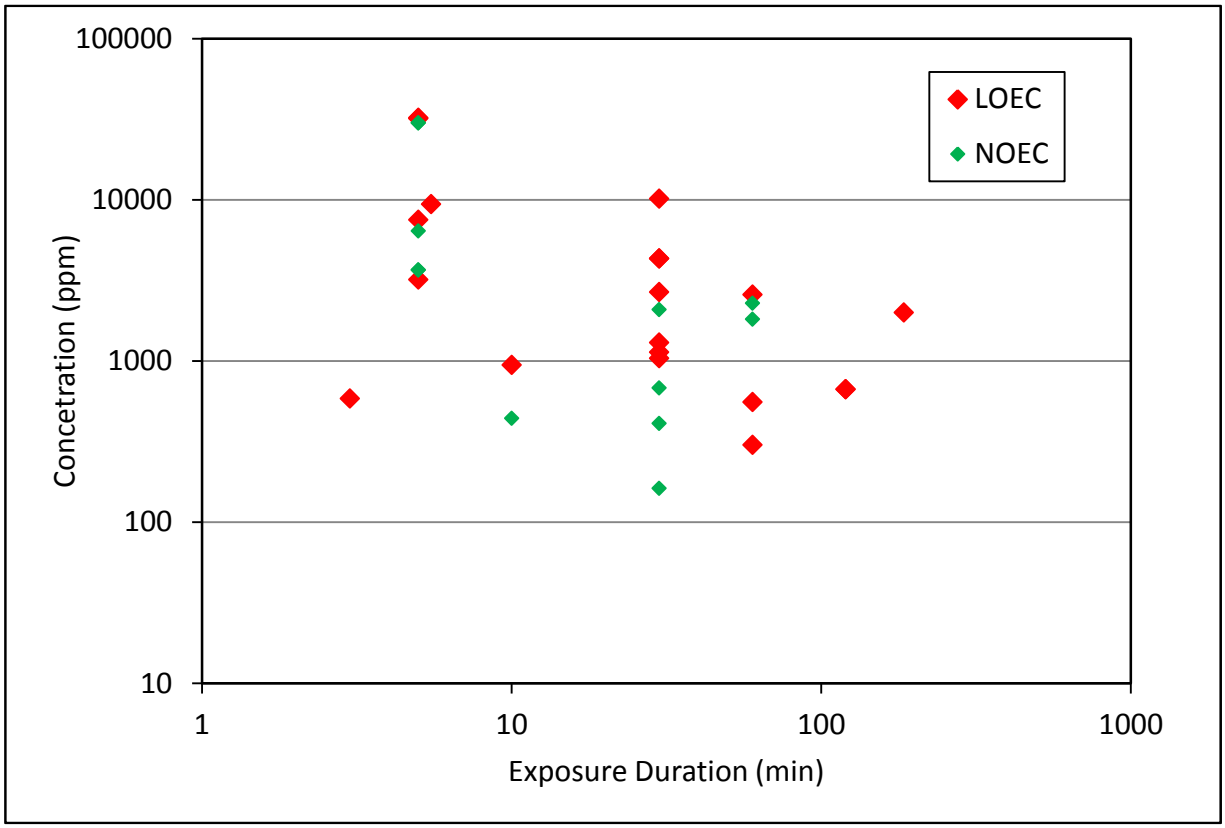

Table B 3-1. Systemic Effects of Short-term Single Exposures of Mammals

Study	Species	ED (min)	Endpoints	NOEC	LOEC (mild)	LOEC (severe)
Barrow et al. 1977	Mouse	10	Decreased respiration	40	245	309
Barrow et al. 1979	Mouse	10	Dec.resp., nasal ulceration		50	120
Kaplan et al 1988	Baboon	5	Coughing, eye irritation	190	810	
Kaplan et al 1988	Baboon	15	Bronchconstriction		500	
Kaplan et al 1993	Guinea Pig	15	Bronchconstriction		500	
Kaplan et al 1993	Rat	15	Decreased respiration		3890	
Kaplan et al 1993	Mouse	15	Decreased respiration		475	
Stavert et al 1991	Rat	30	Nasal lesions, body weight			1293
Burleigh-Flayer et al 1985	Guinea pig	30	Pulmonary irritation		320	1040
Malek and Alarie 1989	Guinea pig	30	Irritation		107	
Malek and Alarie 1989	Guinea pig	16	Incapacitation			140
Hartzel et al 1985	Rat	30	Decreased respiration		200	
Lucia et al. 1977	Rat	10	Resp tract lesions		17	723

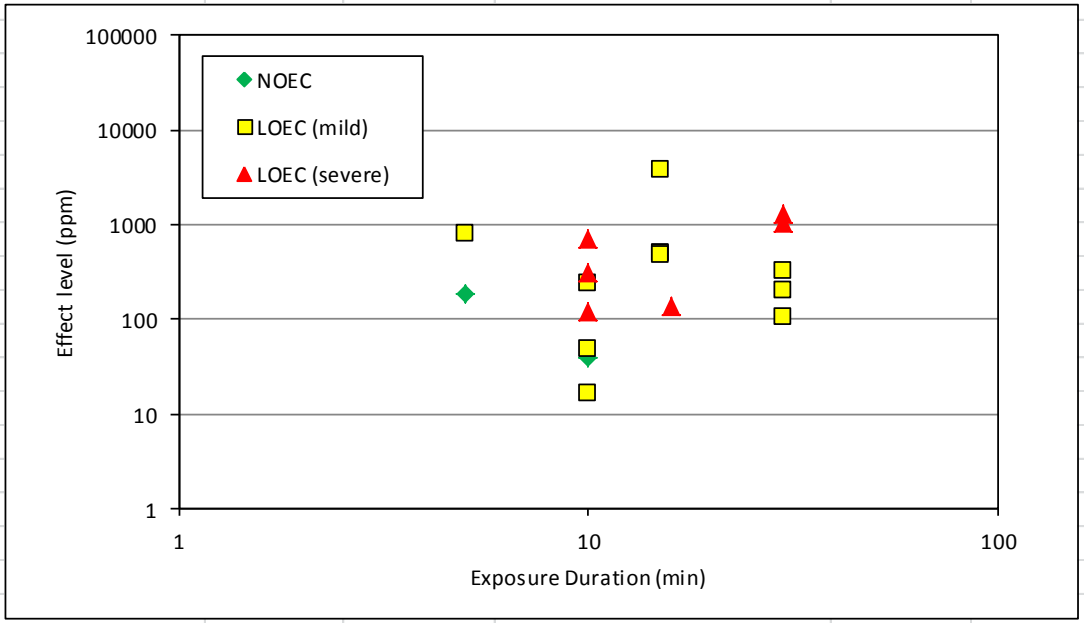

Table B 3-2. Systemic Effects of Repeated Exposures of Mammals

Reference	Species	Endpoint	ET (hrs/day)	EF (days/wk)	ED (days)	NOEC (ppm)	Mild LOEC (ppm)	Serious LOEC (ppm)
Albert et al 1982 (a)	Rat	Hyperplasia of nasal and tracheal epithelium	6	5	Lifetime		10	
Toxigenics 1984	Rat	Slight weight loss	6	5	90	20	50	
Buckley et al 1984	Mouse	Mortality	6	5	3			309
(a) Discussed in Sellakumar et al. 1985								

Table B 3-3.
Selected TRVs (ppm) for Exposure of Ecological Receptors to HCl

Receptor Group	Exposure Duration	Exposure Frequency	Endpoint	
			Nasal/Resp. Tract Injury	Lethality
Mammals	10-30 min	Infrequent	100	300
	6-8 hr	Infrequent	8.3	100
	6-8 hr	Repeated	3	30
Birds	10-30 min	Infrequent	30	100
	6-8 hr	Infrequent	3	30
	6-8 hr	Repeated	1	10

REFERENCES

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EPA RESPONSES 23 August 2014
To

PRELIMINARY REVIEW QUESTIONS/COMMENTS FROM
ERM email of 16 Sep 2014

Regarding
EPA Draft OU-2 Phase 1B DQOs for US Magnesium RI

1. Step 5.1, Step 1, Pages 3 and 4. This section references Appendices A and B, which summarize the data and regulatory guidelines for Cl2 and HCl, respectively. Appendices A and B were not attached to the QAPP or forwarded to us in the email. Please forward these appendices as we cannot review and comment on proposed acute inhalation values for Cl2 and HCl until they have been reviewed.

Appendices A and B have been provided to ERM (see 9 Sep 2014 email from Catherine LeCours).

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Step 5.1, Step 1, Pages 3 and 4. Tables 11-1 and 11-2 are referenced in this section and summarize Acute Exposure Guideline (AEGL) values protective of human exposures, and toxicity reference values for ecological receptors, respectively. Each table presents multiple exposure durations and severity of effects. It is not clear from the text which values EPA is proposing to use. Since the selected values are dependent on the exposure duration and severity of effect, the rationale for the selection of the specific values is critical to understanding the rest of the DQOs (especially as it relates to the exposure duration "d" used to calculate exposure in Steps 5.1 and 5.2). Please provide a detailed discussion of what specific values are proposed and why.

The choice of which AEGL or other RBC values that is/are optimal for risk characterization and decision-making will be made after data are obtained on the magnitude and frequency of spikes occurring at the various monitoring stations.

2. Step 5.1, Step 2, Page 4. Please clarify the rationale for adjusting the measured concentration using Haber's Rule or ten Berge et al. when the RBCs have already been corrected.

If the RBC is derived using the equation recommended by ten Berge, then the concentration values compared to the RBC must also be calculated in the same way.

3. Step 5.1, Step 5, page 7. Please provide additional rationale and the basis for the site-specific Exposure Frequency Goals (EFGs) provided in the small embedded table. Which severity of effect are we managing? How do these specifically relate back to the selected toxicity values (both human and eco)? Is there any precedence for the values selected?

As stated, the EFGs are based on risk management judgments. EPA will seek to limit the frequency of exceedances to the EFG for each severity level. The relation of severity to toxicity data is described in Appendices A and B. EPA is not aware of any precedents.

4. Step 5.2, page 9-10. Please provide further clarification regarding the selection of the chronic Cl2 and HCl RBC value. Is EPA proposing the PALs or IRIS/ATSDR values? If PALs are the selected values, which duration and level of severity is proposed?

EPA considers both the PALs and the IRIS/ATSDR values to be applicable. The PALs will be used for scenarios with exposure durations of several years, while the IRIS/ATSDR values will be used for chronic exposure scenarios.

5. Location of Monitoring Stations, page 12. We cannot find any rationale in Worksheet 11 of the QAPP as to the number of required stations. Please provide rationale as to why 12 monitoring stations are needed.

The position of monitoring stations is based on a consideration of areas where humans and/or ecological receptors may be exposed, seeking to provide good spatial coverage, EPA has sought to select a pattern of stations that are not so close as to be "redundant" ,but not so far apart that there would be a substantial data gap between stations. Because the placement of stations involves judgment, EPA anticipates that discussions with ERM will be appropriate to ensure the final pattern is optimal.

6. Minimum Sampling Duration, page 13. Please provide additional explanation about how Figure 11-2 was created, with references if applicable.

The basic equations needed to generate Figure 11-2 are shown on page 11-13. The detailed calculations are presented in the attached spreadsheet ("Figure 11-2.xlsx").

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